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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/522,731

01/28/2005

Yoshihiko Kotake

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EXAMINER

RAHMANI, NILOOFAR

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 01/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/522,731

Applicant(s)

KOTAKE ET AL.

Examiner

Niloofar Rahmani

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 and 25-55 is/are rejected.
- 7) ☐ Claim(s) 23-24 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-55 are pending.

2. ***Priority***

This application is a 371 of PCT/JP03/09753, filed on 07/31/2003. The claimed benefit of priority date is denied. There is no certified translation of the priority document.

3. ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 47-50 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). These claims are withdrawn from consideration.

4. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22, 25-43, 51-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 25, 27-43 are rejected because the term "medicament" is confusing. Does it mean pharmaceutical composition? Correction is required.

Claim 26 is rejected because the claims are self-conflicting.

Pharmaceutical compositions by definition must be effective yet non-toxic.

Claims 24-25 are pharmaceutical compositions without dosage limitation i.e. included both ineffective and toxic amount. It is recommended that "therapeutically effective amount" be incorporated in the claims.

Claims 1-22 are rejected because the term "hydrate of those" is confusing. What does it mean by those? It is recommended to correct to hydrate thereof.

Claims 27-29, and 34-35 are rejected because it is vague and ambiguous. Is it a claim of method for treating diseases or a claim of pharmaceutical compositions with therapeutically effective amount?

Claims 51-53 are rejected because the term "6-deoxy 11107" is undefined. What is 6-deoxy 11107? It is recommended to define it.

Claims 52, and 54-55 are rejected because the term "strain-A-1543 (FERM BP-8442)" is undefined. What is strain-A-1543 (FERM BP-8442)? It is recommended to define it.

Claim 53 is rejected because the term "biologically converting" is undefined. What is biological converting means? Is it enzyme or another microorganisms? Correction is required.

5. Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22, and 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification lacks description of the claims i.e. "hydrate of them". Hydrate is unpredictable because there are different hydrates. There are $\frac{1}{2}$ hydrate, 3 hydrates, or $\frac{3}{4}$ hydrate, etc. Therefore, the specification lacks description of "hydrate of them".

Claim 44 lacks description of the claim i.e. "treating or preventing a disease against which a regulation of gene expression is effective". Applicant has not shown the nexus for regulation of gene expression and treating or preventing any and all known or unknown diseases. In addition, what diseases are treatable or preventable by gene expression? Therefore, the specification lacks description of "treating or preventing a disease against which a regulation of gene expression".

Claim 45 lacks description of the claim i.e. "treating or preventing a disease against which suppression of VEGF production is effective". On page 136, Table 1 of the specification, applicant has example VEGF transcription-inhibitory activities. However, applicant has not shown the nexus for VEGF

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production and treating or preventing any and all known diseases. In addition, what diseases are treatable or preventable by VEGF production? Therefore, the specification lacks description of "treating or preventing a disease against which suppression of VEGF production is efficacious".

Claim 46 lacks description of the claim i.e. "treating or preventing a disease against which an angiogenesis inhibition is effective". Applicant has not shown the nexus for angiogenesis inhibition and treating or preventing any and all known or unknown diseases. In addition, what diseases are treatable or preventable by angiogenesis inhibition? Therefore, the specification lacks description of "treating or preventing a disease against which an angiogenesis inhibition is efficacious".

Claim 51 is rejected under 35 U.S.C. 112, first paragraph. The claim lack operable steps and parameter. The claim encompassed any and all conditions and the whole genus *Streptomyces* for producing a 6-deoxy 11107 compound from culturing a microorganism belonging to the genus *Streptomyces* for which insufficient description was found in the specification for all conditions and all for the genus.

6. Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 51-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To satisfy the enablement requirement a deposit must be made "prior to issue" but need not be made prior to filing the application. *In re Lundak*, 773 F.2d 1216, 1223, 227 USPQ 90, 95 (Fed. Cir. 1985).

Claims 51-55 are drawn to microorganism belonging to the genus *Streptomyces* with no limitation to the species. There is no record for any deposit in the prosecution record. What species in the genus *Streptomyces* makes the compound or do the entire genus *Streptomyces* make the compound? If so, then enablement is needed for that. Any species embraced by the genus including future development must be deposited in compliance with MPEP§ 2404.

7. Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 44 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compound to alter the gene expression and therefore to treat any and all known or unknown diseases. The claim contains subject matter,

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which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to compounds, which show preventing or treating a disease for which gene expression control is effective.

The state of the prior art: Gene therapy is emerging as a potential strategy for the treatment of cardiovascular diseases, such as peripheral arterial disease (PAD), ischemic heart disease, restenosis after angioplasty, vascular bypass graft occlusion and transplant coronary vasculopathy with vascular endothelial growth factor (VEGF) (Ryuichi Morishita, Circ Journal, vol. 66, pages 1077-1086).

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be used for preventing or treating a disease for which gene expression control is effective.

Amount of guidance/working examples: Applicant provides no guidance for how gene expression control could treat or prevent any and all known or unknown diseases. Nor does applicant identify what diseases are treatable by gene expression control.

There are no examples in the instant specification showing that the instant compounds control gene expression. Nor are there any examples of the diseases being either treated or prevented by gene expression control.

The breadth of the claims: The breadth of claims is drawn to treating or preventing any and all known or unknown diseases associated with gene expression control.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating or preventing diseases against which gene expression control is effective, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claim 44, for treating or preventing diseases against which gene expression control is effective, have been enabled by the instant specification.

8. Claim 45 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compound to alter the suppression of VEGF production and therefore to treat any and all known or unknown diseases. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,

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- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to compounds, which show preventing or treating a disease against which suppression of VEGF production is effective.

The state of the prior art: The trophoblast-link choriocarcinoma cell line BeWo expresses a receptor for vascular endothelial growth factor (VEGF) and proliferates in response to VEGF (Moon-Seok Cha, Biochemical and Biophysical Research Communications, vol. 282, pages 1061-1066).

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed

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invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be used for treating or preventing diseases against which suppression of VEGF production is effective.

Amount of guidance/working examples: Applicant provides no guidance for how suppression of VEGF production could treat or prevent any and all known or unknown diseases. Nor does applicant identify what diseases are treatable by suppression of VEGF production.

There are no examples in the instant specification showing that the instant compounds suppress VEGF production. Nor are there any examples of the diseases being either treated or prevented by suppression of VEGF production. On page 136, Table 1 of the specification show the instant compounds for VEGF transcription-inhibitory but this is not the suppression of VEGF production.

The breadth of the claims: The breadth of claims is drawn to treating or preventing any and all known or unknown diseases associated with suppression of VEGF production.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating or preventing diseases against which suppression of VEGF production is effective, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claim 45, for treating or preventing diseases against which suppression of VEGF production is effective, have been enabled by the instant specification.

9. Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compound to alter an angiogenesis inhibition and therefore to treat any and all known or unknown diseases. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the

inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to compounds, which show preventing or treating a disease against which an angiogenesis inhibition is efficacious.

The state of the prior art: Inhibition of skin angiogenesis can prevent UVB-induced skin damage, e.g., long term (chronic) UVB induced photoaging, e.g., wrinkle formation, in vivo, in mammals, e.g., humans. A method for preventing or treating long-term UVB-induced skin damage, e.g., wrinkles includes inhibiting angiogenesis in the skin (US 6,712,617).

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the

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art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be used for treating or preventing diseases against which an angiogenesis inhibition is efficacious.

Amount of guidance/working examples: Applicant provides no guidance for how angiogenesis inhibition could treat or prevent any and all known or unknown diseases. Nor does applicant identify what diseases are treatable by angiogenesis inhibition.

There are no examples in the instant specification showing that the instant compounds angiogenesis inhibition. Nor are there any examples of the diseases being either treated or prevented by angiogenesis inhibition.

The breadth of the claims: The breadth of claims is drawn to treating or preventing any and all known or unknown diseases associated with angiogenesis inhibition.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating or preventing diseases against which an angiogenesis inhibition is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claim 46, for treating or preventing diseases against which an angiogenesis inhibition is effective, have been enabled by the instant specification.

10. *Double Patenting*

Claim 26 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 25. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The preamble does not give patentable weight to the claim.

11. *Claim Objections*

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Claims 23-24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI

01/02/2006

NR


D. MARGARET SEAMAN

PRIMARY EXAMINER

GROUP 1625